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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 02/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/129,758	WALDMANN ET AL.	
	Examiner	Art Unit	
	Nirmal S. Basi	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,11-13,15,17-23,26 and 27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 11-13, 15, 17-23, 26-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/7/05 has been entered.

2. Amendment filed 12/7/05 has been entered. Claims 1, 11-13, 15, 17-23, 26-27 are pending.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejection, 35 U.S.C. 112

4. Amended claims 1, 11-13, 15, 17-21 and 26-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "the amino acid sequence" in line 3. There is insufficient antecedent basis for this limitation in the claim. Claim 1 is indefinite because it is not clear if the "the amino acid sequence" in line 3 refers to the claimed isolated and purified protein or if the amino acid sequence used is to select the “part” of the ASIC channel.

Claim 11 is indefinite because it is not clear if the nucleic acid molecule is isolated and purified or only the nucleic acid sequence is

isolated and purified. It must be noted that the nucleic acid sequence can be merely letters on a page. It is suggested to overcome the rejection that the claim be amended to "An isolated and purified nucleic acid molecule comprising the nucleic acid sequence encoding the protein of claim 1".

Claims 12-13, 15, 17-21 and 26-27 are rejected for depending upon an indefinite base.

Claim Rejections - 35 USC 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claim 11 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claim 11 recites a nucleic acid molecule but do not recite that it is isolated or purified. The claim as currently recited encompass naturally-occurring compounds. Therefore, the compounds as claimed are a product that occurs in nature and does not show the hand of man, and as such is non-statutory subject matter. It is suggested that the claims be amended to recite an isolated and purified nucleic acid molecule to overcome this rejection. The amendment of the claim to "isolated and purified nucleic acid sequence" is insufficient to overcome the rejection of record. It must be noted that the nucleic acid sequence can be merely letters on a page. Since the nucleic acid molecule is

being claimed, said nucleic acid molecule must be one that is shown to be "isolated and purified"

Claim Rejection, 35 U.S.C. 112 (New matter)

6. Claim 1 remains rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 1 recites "part or all" of a mammalian neuronal cationic ASIC channel selected from the group of SEQ ID NO:2, 4 or 8. Applicants arguments state support for the amendment of claim 1 is found on page 4, lines 1-8. Examiner can find no support for "part". Applicant argues "hybrid" constitutes "part". Applicant's arguments have been fully considered but are not found persuasive. Applicants refer to the following passage (page 4) for support for "part":
"The invention also relates to a hybrid cationic channel constituted by the combination of a first protein constituting a proton-activated ionic channel according to the invention with a second protein constituting a proton-activated ionic channel. Advantageously, the second protein is also a protein constituting a proton-activated ionic channel according to the invention. As an example of such a combination, one can cite the combination of the protein of the ASICIA or ASICZA or DRASIC channel with the protein of the MDEGI channel, enabling formation of a hybrid channel . . ."

Nowhere in the recited passage does it refer to the claimed protein comprising a "part" of an ASIC channel. Even the recited examples do not refer to "part". The specification supports the combination *"a first protein constituting a proton-activated ionic channel according to the invention with a second protein constituting a proton-activated ionic channel".*

Appropriate correction of the claim is required to overcome the new matter rejection.

7. Claims 1, 11-13, 15, 17-23, 26-27 remain rejected under 35 U.S.C. 101, for reasons of record (4/6/05), because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Applicants arguments pertaining to the rejection of claims 1, 11-13, 15, 17-23, 26-27 under 35 U.S.C. 101 and 112, first paragraph are summarized below:

Applicants argue ASIC channels, expressed throughout the brain, conduct the flux of ions through the membranes of cells. The family of ion channel proteins is responsible for a number of specific cellular activities including the propagation of nerve impulses and a number of neurodegenerative diseases. ASIC channels are activated by extracellular acidification and associated with a number of activities (nociception, taste transduction, anxiety disorder, pathaologies such as cerebral neuronal degeneration), and these activities can readily be used by those skilled in the art. Applicants' arguments have been fully considered but are not found persuasive. The general activity of ion transport, possessed by the family of channel proteins, cannot be used to support utility in instant case. A detailed argument to Applicants' traversal is provided below.

Applicants argue Amiloride-sensitive degenerine sodium channels are associated with molecular defects and they can be used as a target for therapeutics. Applicants also argue the art has clearly recognized the role of Amiloride-sensitive degenerine sodium channels in neurons and their correlation to disease states. Applicants argue ASIC channels can be used to detect a disease state. Applicants also argue antagonists of ASIC channel can be used to treat stroke by blocking ASIC channel activity. Applicants' arguments have been fully considered but are not found persuasive. In light of the specification the skilled artisan can conclude that protein of instant invention is a cationic channel protein. However, no disclosure is provided within the instant specification on what specific function the claimed cationic channel protein possess, nor are any disease states disclosed that are directly related to claimed channel dysfunction. A detailed argument to Applicants' traversal is provided below.

The references supplied by applicants clearly show that the role of ASIC protein channels was unknown at the time of filing of instant application. For example, see Chen et al (Proc. Natl. Acad. Sci. USA, Vol. 95, pp10240-10245, August 1998), page 10245, column 1, last paragraph, which states ASIC channels have a widespread distribution in the central nervous system but as yet have an unknown physiological role.

Allen at al (J. of Physiology, Vol 543 (2), pages 521-529, 2002), page 521, column 2, discloses little is known about the modulation of ASIC channels in the

central neurons, ASIC channels require a large and rapid fall of pH to be activated and it is unclear when this might happen in the CNS.

Wemmie et al (The Journal of Neuroscience, Vol. 23, (13) pages 5496-5502, 2003) page 5502, column1 discloses additional studies will be necessary to delineate the multiple possible effects of ASIC on behavior.

Baron et al (journal of Physiology, Vol 539(2), pages 485-494, 2002) page 485 discloses ASIC are functionally diverse and the role of ASIC1a, ASICa, ASIC2b and ASIC4 in the central neurons remains to be established. Therefore based on the art and the specification the role of claimed channel and its association with a specific disease or dysfunction was unknown at the time of filing of instant application.

Applicants argue description of the Applicants' ASIC channels provides a precise target for the development of therapeutic treatments in physiological systems ranging from the neural to the immune system. Applicants argue the activity patterns of ASIC can be used to screen for therapeutic compounds, which inhibit ASIC activity in localized brain tissue culture. Also argued ASIC can be used for molecular diagnostics. Applicants' arguments have been fully considered but are not found persuasive. Although the family of ASIC proteins domains may share some common structural motifs, various members of the family may have different sites of action and different biological effects. No disease states are disclosed that are directly related to claimed channel dysfunction The specification does not disclose a correlation between any specific disorder and an altered level or form of the claimed polypeptides or

methods of its use. Applicant asserts the claimed invention can be used to cure or diagnose a wide variety of diseases. Applicants' arguments have been fully considered but are not found persuasive. Applicant has provided a laundry list of diseases that may be cured or diagnose but provided no data or nexus between the claimed invention and stated use.

Claimed invention belongs to a family of ion transporting proteins, which have different electrophysiological properties and divergent physiological functions that result from the transport of said ions.

The protein gated channel of instant invention belongs to a complex family of ion channels with varied properties and functions (discussed in office Action, 11/17/03. The observation that claimed invention is an amiloride-sensitive degenerine sodium channel and the disclosure of amiloride sensitivity and certain biophysical properties does not provide support for either a specific and substantial asserted utility or a well-established utility. The specification discloses, pages 2 and 3, the family of structural relatives of ASIC channels (also designated as MDEG) have different electrophysiological properties and that no normal physiological function of said MDEG was known until the demonstration of its activation by protons (also see page 17, lines 13-16). Also disclosed, page 5, inactivation and kinetics and the ionic selectivity of the channel formed after co-expression of different MDEG are different than those if only one channel is expressed. Therefore, expression of the various MDEGs in different tissues may have divergent functional effects due the presence of other channel proteins. The specification, page 5, lines 8-9 states, when referring to claimed

ion channel, this property is very similar to that of the proton-activated cationic channel which is implicated in the prolonged sensation of pain caused by acidosis. It is very probable that DRASIC and MDEG2 are part of this channel. The claimed ion channel is speculated to be similar to the family of proton-activated ion channels, but there is no disclosure in the specification that instant invention is useful for screening substances capable of modulating the perception of acidity regarding both noiception and taste transduction, said substances being further useful in the fabrication of drugs intended for the treatment or prevention of pathologies entailing the painful perception of acidity which interferes in inflammatory diseases. All members of the ASIC family do not have the same electrophysiological properties (ASIC2b, does not respond to low pH, ASIC4 is inactive by itself and hence is not thought to encode a proton-gated ion channel), and members have been proposed to function in a wide variety of disease states e.g. pain sensation, ischemia, epilepsy, neurodegenerative diseases, but their role in the brain in is obscure, see Berdiev et al in previous Office Action, Ref U, page 15023, second column. The function of these channels in the glia remains a mystery; see Berdiev et al, page 15023. Further it has been shown that constitutive amiloride-sensitive currents are a specific feature of the more aggressive brain tumors (see Berdiev et al, page 15034, column 1). Further, amiloride sensitivity cannot be used to infer a specific or well-established utility. Berdiev discloses the difficulty of assigning a function based on amiloride sensitivity. Berdiev, states (page 15034, column 1, second paragraph), "amiloride-sensitive sodium channels cannot easily be classified

based on simple biophysical parameters, such as single channel conductance and/or sensitivity to amiloride. This class of ion channel, both in the brain and in epithelial tissues, appear to have a variable composition, and hence tissue-specific differences in biophysical parameters may result from different channel compositions in different tissues". Further the specification provides no significance of the function of amiloride (a drug that blocks sodium/proton antiport and has been used clinically as a potassium sparing diuretic) as it correlates to it role in pain sensation.

The utilities are not considered to be specific and substantial because the specification fails to disclose any particular function or biological significance for the ion channel of the instant invention. The disclosed protein, whose cDNA has been isolated, is said to have a potential function based upon its amino acid sequence similarity to other known proteins. After further research, a specific and substantial utility might be found for the claimed isolated compositions. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicants claimed invention is incomplete. In light of the specification the skilled artisan can conclude that protein of instant invention is a cationic channel protein. However, no disclosure is provided within the instant specification on what specific function the claimed cationic channel protein possesses, nor are any disease states disclosed that are directly related to cation channel dysfunction. Ions are known to play a role of first or second messenger in numerous cellular signaling contexts, but it is not known what role claimed cationic channel plays in signaling and what would be the use of interfering with

its function, apart from as targets for drug discovery. Further it is not clear from the specification if the channel protein disclosed by the amino acid sequence of SEQ ID NO: 4 encoded by SEQ ID NO: 3 has ion transport activity. There is no disclosure in the specification, which shows the protein of SEQ ID NO: 4 was assayed for activity.

The utilities asserted by Applicant are not specific or substantial. Since no specific function of claimed cation channel is known, and the ability to transport ions with no associated function is not considered a well established utility, the hypothesized functions are based entirely on conjecture from homologous polypeptides. The asserted utilities are not specific to instant polypeptide, but rather are based on family attributes. Neither the specification nor the art of record disclose any compounds that treat a specific disorder associated with dysfunction of the nucleic acid of SEQ ID NO: 1, 3 or 8 or its encoded protein (SEQ ID NO: 2, 4 or 8). Similarly, neither the specification nor the art of record disclose any instances where disorders can be affected by interfering with the activity of claimed cation channel. Thus the corresponding asserted utilities are essentially methods of using claimed cation channel to identify or treat disease states associated with cation channel polypeptide dysfunction and as targets for drug discovery. Therefor the asserted utilities are essentially methods of testing for or for potentially treating unspecified, undisclosed diseases or conditions, which does not define a "real world" context of use. Treating or testing for compounds that interact with claimed cation channel, which may be implicated in an unspecified, undisclosed disease or

condition would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. Since neither the specification nor the art of record disclose any activities or properties that would constitute a Areal world≅ context of use for the claimed cation channel, further experimentation is necessary to attribute a utility to the claimed cation channel. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are Auseful≅ to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of useful as it appears in 35 U.S.C. 101, which requires that an invention must have either an immediately apparent or fully disclosed real world utility. The court held that:

The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion.

The DNA of the instant invention and the protein encoded thereby are compounds, which share some structural similarity to other ion channel proteins based on sequence similarity. The family of proteins related to instant invention may have diverse effects and bind a diverse number of ligands (e.g. syntax , see Berdiev et al). Although the family of ASIC proteins domains may share some common structural motifs, various members of the family may have different sites of action and different biological effects. The specification does not disclose a correlation between any specific disorder and an altered level or form of the claimed polynucleotides/polypeptides. Also, the specification does not predict whether the claimed polynucleotides/polypeptides would be over expressed or under expressed in a specific, diseased tissue compared to the healthy tissue control. The specification contains assertions that the claimed polynucleotides/polypeptides can be used the art for drug development. However, without a disclosure of a particular disease state in which the claimed polynucleotides/polypeptides are expressed at an altered level or form, it would be impossible to determine what the results of a gene expression/protein expression monitoring assay mean. For example, if a compound is tested on a microarray comprising the claimed polynucleotides and affects expression of the polynucleotides negatively, it cannot be determined if that means that the compound is a potential good drug for a disease or would acerbate the disease if administered. The test results also would not have meaning in terms of what specific disease is relevant. Further, before the claimed invention can have utility in gene expression, significant, further research would have to be conducted to

determine which diseases correlate with altered forms or levels of the claimed polynucleotides, and whether the claimed polynucleotides are over expressed or under expressed in the diseased tissue. The disease state itself has to be identified.

The proposed uses of the claimed invention are simply starting points for further research and investigation into potential practical uses of the claimed nucleic acids/polypeptides. Even if the expression of Applicants individual polynucleotides/polypeptides are affected by a test compound in an array for drug screening, the specification does not disclose any specific and substantial interpretation for the result, and none is known in the art. Given this consideration, the individually claimed polynucleotides have no "well-established" use. The artisan is required to perform further experimentation on the claimed material itself in order to determine to what "use" any expression information regarding this nucleic acid could be put.

If a molecule is to be used as a surrogate for a disease state (e.g. gene therapy), some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polynucleotide to be used in a diagnostic manner. Many proteins are expressed in normal tissues and diseased tissues. Therefore, one needs to know, e.g., that the claimed polynucleotide is either present only in cancer tissue to the exclusion of normal tissue or is expressed in higher levels in diseased tissue compared to normal tissue (i.e. over expression). In instant case Applicants implicate Alzheimer's disease. Is claimed DNA/protein over-expressed or under expressed

in Alzheimer's disease? There is no data in specification or prior art that provides support for the claimed ion channel dysfunction resulting in Alzheimer's disease. Evidence of a differential expression might serve as a basis for use of the claimed polynucleotides as diagnostics/treatment for diseases. However, in the absence of any disclosed relationship between the claimed polynucleotides or the proteins that are encoded thereby to any disease or disorder and the lack of any correlation with any known disease or disorder, the use of ASIC gene, or its encoded polypeptide, in therapy, would only serve as the basis for further research. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner v. Manson*, 148 USPQ at 696. The disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. §101.

The ASCI family is functionally highly diverse. When there is great functional diversity in a structurally related class of compounds, the class cannot be used to predict a utility for a new compound that fits in the class by structural similarity. Such is the case here. The specification has not disclosed a specific disease or disorder of any type wherein the claimed polynucleotides/polypeptides are expressed at altered amounts or forms relative to the required control healthy tissue. Significant further research would be required of the skilled artisan to identify such a disease or disorder. Therefore the asserted utility is not substantial. The polypeptide encoded by the polynucleotide belongs to a family in which the members have divergent functions based on which tissues the

protein is expressed or administered to. Assignment to this family does not support an inference of utility because the members are not known to share a common utility. There are some protein families for which assignment of a new protein in that family would convey a specific, substantial and credible utility to that protein. For example, some families of enzymes such as proteases, ligases, telomerases, etc. share activities due to the particular specific biochemical characteristics of the members of the protein family such as non-specific substrate requirements, that are reasonably imputed to isolated compositions of any member of the family. Although the ASIC belongs to a family of proteins that transport ions, the family has divergent functional effects as consequence of that ion transport, and cannot be compared to the ligase family of proteins, which have a specific effect, ligate DNA.

8. Claims 1, 11-13, 15, 17-23, 26-27 remain rejected under 35 U.S.C. 112, first paragraph, for reasons of record (see previous Office Action) . Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above and in the previous Office Action, one skilled in the art clearly would not know how to use the claimed invention. Since neither the specification nor the art of record disclose any activities or properties that would constitute a real world context of use for the claimed cation channel, further experimentation is necessary to attribute a utility to the claimed polypeptides, polynucleotides and methods of their use.

9. Amended claims 1, 11-13, 15, 17-23 and 26-27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant specification does not contain a written description of the invention in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing. The claims are directed to an isolated and purified protein constituting **part or all** of a mammalian neuronal cationic ASIC channel that is sensitive to amiloride and activated by protons, wherein the amino acid sequence is selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 4, and SEQ ID N0: 8. Claims are also drawn to nucleic acid encoding claimed ASIC channel, vectors comprising said nucleic acid, cell comprising said vector, and methods of their use. It is not clear from the claim language if the claimed isolated and purified ASIC channel is sensitive to amiloride and activated by protons or that merely a part of said channel has to be present in the isolated and purified protein regardless of whether or not it retains its activity when contained in the claimed product. The protein/nucleic acid as claimed encompasses products that do not require sensitivity to amiloride and activatation by protons, absent evidence to the contrary.

The specification discloses the polypeptide of SEQ ID NO:2, 4 and 8 encoded by the polynucleotide of SEQ ID NO:s 1, 3 and 7. There is no

disclosure of the "part" of the mammalian neuronal cationic ASIC channel that senses amiloride and is activated by protons. Further, it is not clear from the specification if the partial channel protein disclosed by the amino acid sequence of SEQ ID NO:4 encoded by SEQ ID NO:3 is functional. The channel protein of SEQ ID NO:4 is considered by Examiner to lack functionality, absent evidence to the contrary. There is no disclosure in the specification, which shows the protein of SEQ ID NO:4 was assayed for activity. The instant disclosure of three distinct polypeptide does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera including full-length, truncated, fusion molecules and variants thereof; the The claims encompass polypeptides and polynucleotides which contain "part or all" the compounds disclosed in SEQ ID NO:2, 4, or 8, which encompasses, mutants, variants, analogs, homologs or derivatives of SEQ ID NOS:2, 4 and 8. There is no disclosure of the "part" of SEQ ID NOS:2, 4 and 8, which contains the required functionality. Further claims 22-23 and 28-29 provide no structural information about the ASIC channel used in the claimed methods.

A description of a genus of polypeptides/polynucleotides may be achieved by means of a recitation of a representative number of polypeptides, defined by an amino acid sequence/nucleic acid sequence, falling within the scope of the genus or of a recitation of structural and functional features common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant specification fails to

provide sufficient descriptive information, such as definitive structural and functional features of the claimed genus of polypeptides and polynucleotides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. The fusion polypeptides, fragments and variants encompassed by the claims do not disclose the critical technical feature of the claimed invention or its relationship to function. For example, polypeptides comprising a fragment or variants of SEQ ID NO:2, 4 and 8 may be completely unrelated to the disclosed polypeptide of SEQ ID NO: 2, 4 and 8, having a different functional properties. The critical technical feature encompassed by the fragments (parts) and variants must relate to the encompassed polypeptide, structurally and functionally to the disclosed proteins of SEQ ID NO:2, 4 and 8. The same argument applies to the mutants, variants, analogs, homologs, derivatives and fusion products encompassed by the claims. It is not clear what critical technical feature undisclosed amino acids, disclosed amino acids in a specific fragment, or recited descriptive language provide so as to show a written description of the invention in full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing. There is no description, of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and

identify the polynucleotides encompassed and no identifying characteristic or property of the encoded polypeptides is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

The specification further fails to identify and describe the regulatory regions essential to the function of the claimed invention, which are required since the claimed invention currently encompasses the full length, truncated, fusion products and variants thereof. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus may be highly variant, the disclosure is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

An adequate written description of a protein or nucleic acid molecule requires a precise definition, such as by structure, formula, chemical name, and physical properties, not a mere wish or plan for obtaining the claimed chemical invention. Accordingly, an adequate written description of a polypeptide is more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the polynucleotide or the encoded protein itself. Accordingly, the specification does not provide a written description of the invention of claims 1, 11-13, 15, 17, 18-23 and 26-29.

The critical special technical feature of the polypeptides/polynucleotide or how the critical special technical feature

encompassed by the genus claimed relates to function is not disclosed. The name ASIC cationic channel provides no structural information about the claimed channel and encompasses compounds which may have variant functional properties.

The breadth of the claim come from encompassing polynucleotide encoding a protein, the fragments or variants which do not have an associated structure which defines the critical special technical feature of the invention. *Vas-Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid or polypeptide is itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

With the exception of SEQ ID NO:2, 4 and 8, the skilled artisan cannot envision the detailed chemical structure of the claimed polypeptide and polynucleotides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not achieved. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGFs were found unpatentable due to lack of written description for the broad class.

Therefore, only the polypeptide comprising SEQ ID NO:2, 4 and 8, the nucleic acid comprising SEQ ID NOs: 1, 3 and 7, vectors containing said nucleic acid, cells containing said vector and methods using said polypeptide, nucleic acid, vector, cell but not the full breadth of the claim meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115). 8

10. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal S. Basi whose telephone number is 571-272-0868. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art Unit 1646
2/21/06

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER